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Hilar Cholangiocarcinoma

Patterns of Spread, the Importance of Hepatic Resection for Curative Operation, and a Presurgical Clinical Staging System

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Objectives
To determine the resectability rate for hilar cholangiocarcinoma, to analyze reasons for unresectability, and to devise a presurgical clinical T-staging system.

Methods
Ninety patients with hilar cholangiocarcinomas seen between March 1, 1991, and April 1, 1997, were evaluated. Accurate patterns of disease progression and therapy were evaluable. Disease was staged in 87 patients using extent of ductal tumor involvement, portal vein compromise, and liver atrophy.

Results
In 21 patients, disease was deemed unresectable for cure at presentation. In 39 patients, disease was found to be unresectable at laparotomy, 23 secondary to nodal (N2) or distant metastases. Unresectability was the result of metastases in 52% and of locally advanced disease in 28%. Thirty patients (33%) had resection of all gross disease, and 25 of these (83%) had negative histologic margins. Twenty-two patients underwent partial hepatectomy. The 30-day mortality rate was 7%. Projected survival is greater than 60 months in those with a negative histologic margin, with a median follow-up of 26 months. A presurgical T-staging system allows presurgical selection for therapy, predicts partial hepatectomy, and offers an index of prognosis.

Conclusions
In half the patients, unresectability is mainly the result of intra-abdominal metastases. Presurgical imaging predicts unresectability based on local extension but is poor for assessing nodal metastases. In one third of patients, disease can be resected for cure with a long median survival. Curative resection depends on negative margins, and hepatic resection is necessary to achieve this. The T-staging system correlates with resectability, the need for hepatectomy, and overall survival.

Cholangiocarcinomas involving the confluence of the hepatic ducts are rare, representing less than 2% of all cancers.[1,2] Their location at the upper hepatoduodenal ligament, their extension into the liver, and their proximity to major vascular structures render them difficult to evaluate before surgery and at laparotomy.[3] Meaningful experience with these tumors has been limited, and in many institutions, departmental organization may not allow all patients to be seen or treated by the same service. An accurate accounting of all patients seen, with both resectable and unresectable disease, and the therapy rendered has thus been difficult to establish.

Most reported studies on hilar cholangiocarcinoma are surgical series that do not address unresectable disease, and surgical findings precluding resection are seldom detailed. Reported resectability rates vary from 10% to 50%,[4–9] with most authors defining curative resection as one resulting in the removal of all gross disease.[6–8] The significance of positive histologic margins has been debated in the recent past,[8,10,11] although evidence is mounting that resection achieving negative histologic margins confers a survival advantage.[5,9,10]

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The Bismuth–Corlette classification stratifies patients based on the extent of biliary ductal involvement by tumor[12] but is not a staging system and does not take into account lobar atrophy and vascular invasion. A presurgical system is desirable that stratifies patients into subgroups with some prediction of resectability, the need for hepatic resection, and survival.

At Memorial Sloan-Kettering Cancer Center (MSKCC), the hepatobiliary program consists of physicians from the hepatobiliary surgical service, gastrointestinal, and medical oncology services and the departments of surgery and radiology. At biweekly meetings, all patients with hepatobiliary disease are evaluated and comprehensive treatment plans formulated. Regardless of stage of disease, treatment options are selected on a multidisciplinary basis. This system enables a review of all stages of disease at presentation, including surgical and nonsurgical candidates.

We reviewed our experience to determine:

- The curative resection rate of all patients with hilar cholangiocarcinoma compared to those considered before surgery to have potentially resectable disease
- The factors that make disease unresectable for cure at presentation and at laparotomy
- The results of curative resection in this disease and possible approaches to improve treatment.

We also attempted to develop a model based on presurgical imaging data that stratifies patients into treatment groups with predictable resectability rates and some estimate of survival.

MATERIALS AND METHODS

All patients with hepatobiliary disease evaluated at MSKCC are entered into the data base of the hepatobiliary service of the department of surgery. A list of 225 patients with a diagnosis of cholangiocarcinoma was retrieved from this data base dating from March 1, 1991, to April 1, 1997. Ninety patients had hilar cholangiocarcinoma, defined as tumors originating in the common, right, or left hepatic duct. Papillary cholangiocarcinoma was considered hilar if the base of the tumor originated in the bile ducts defined above. Patients with diffuse bile duct involvement were included if the confluence was involved and no gallbladder or pancreatic mass was identified. The initial consultation notes, imaging reports, surgical records, pathology reports, discharge summaries, and follow-up visits were reviewed and data coded for presurgical resectability, surgical procedure and intent, pathology, hospital stay, and complications. Patients who underwent resection of all gross disease had complete follow-up.

Patients were grouped into one of two categories according to the initial consultation note and imaging studies: unresectable for cure or potentially resectable for cure.

Imaging studies varied among patients because most were referred with at least a partial workup, usually a computed tomographic (CT) scan. For evaluation of longitudinal tumor extent in the bile duct, all patients underwent percutaneous transhepatic cholangiography, endoscopic retrograde cholangiopancreatography, or ultrasound, and more recently magnetic resonance cholangiopancreatography (MRCP). Hepatic ductal involvement was evaluated based on the classification of Bismuth and Corlette.[12] To evaluate radial spread, all patients underwent hepatic angiography (arterial and venous phase) with CT portography or Doppler ultrasound or MRCP. All patients also had a screening chest x-ray before surgery. The current imaging studies favored at MSKCC for presurgical evaluation are Doppler/ultrasound,[13,14] MRCP,[14] and chest x-ray. Hepatic lobar atrophy was considered present if cross-sectional imaging (CT or MRCP) demonstrated a small, often hypoperfused lobe with crowding of dilated intrahepatic ducts.[2] Portal vein involvement was defined radiographically as compression or narrowing, encasement, or occlusion. The presence of lymphadenopathy alone on presurgical imaging was not a contraindication for exploration unless proven histologically to contain tumor.

Table 1. CRITERIA FOR UNRESECTABILITY

Patient factors
Inability to tolerate a major operative procedure
Cirrhosis
Local factors*
Hepatic duct involvement up to secondary radicles bilaterally
Encasement or occlusion of the main portal vein proximal to its bifurcation
Atrophy of one liver lobe with encasement of contralateral portal vein branch
Atrophy of one liver lobe with contralateral secondary biliary radicle involvement
Distant disease
Histologically proven nodal disease
Lung, liver, or peritoneal metastases

* Arterial involvement is not clearly assessable using the imaging modalities commonly employed and was not taken into account as a factor in judgment of irresectability.

The accepted radiologic criteria[15] used to establish unresectability are listed in Table 1, along with other patient factors. All other patients were considered to have potentially resectable disease. Patients were considered to have had a potentially curative resection if all gross disease was resected in the absence of metastases. Patients who underwent a potentially curative procedure, as defined above, were then further stratified into those with negative (R0) and positive (R1) histologic margins.

The presurgical imaging data were also used to determine a T-staging system in 87 evaluable patients, taking into account the extent of local disease irrespective of N or M status (Table 2).

The surgical technique used for the resection of hilar cholangiocarcinoma has been developed by the senior au-

Table 2. PROPOSED T STAGE CRITERIA FOR HILAR CHOLANGIOCARCINOMA

Stage	Criteria
T1	Tumor confined to confluence and/or right or left hepatic duct without portal vein involvement or liver atrophy
T2	Tumor confined to confluence and/or right or left hepatic duct with ipsilateral liver atrophy. No portal vein involvement demonstrated.
T3	Tumor confined to confluence and/or right or left hepatic duct with ipsilateral portal venous branch involvement with/without associated ipsilateral lobar liver atrophy. No main portal vein involvement (occlusion, invasion or encasement)
T4	Any of the following: i) Tumor involving both right and left hepatic ducts up to secondary radicles bilaterally ii) Main portal vein encasement

thor.[2,3,5,15] Exposure of the hepatic confluence for vascular assessment was accomplished by early transection of the common bile duct above the duodenum, with reflection superiorly. Hepatic resection, with or without the caudate lobe, was performed to achieve histologically negative margins. The nomenclature of hepatic resectional procedures is based on the classification of Couinaud.[16] Assessment of margins was obtained during surgery in most cases.

Patient survival was calculated using the Kaplan–Meier estimate. Survival results include deaths secondary to post-surgical complications. Differences in survival between groups was assessed by the log-rank test. $P \leq 0.05$ was considered significant. Survival curves were generated using SPSS version 7.0 (Statistical Package for Social Science, Chicago, IL).

For the T-staging system, categorical variables were compared using chi square analysis. The Bismuth–Corlette classification, portal vein involvement, and hepatic lobar atrophy were further analyzed in a stepwise logistic regression model with resectability and the need for partial hepatectomy as outcome variables.

RESULTS

Two hundred twenty-five patients with cholangiocarcinoma involving the extrahepatic bile ducts were evaluated. Ninety patients (40%) had hilar cholangiocarcinoma (Fig. 1, Table 3). After a full examination and review of all studies, 21 patients were considered to have unresectable disease and 69 patients were considered to have potentially resectable disease. Of those whose disease was unresectable at presentation, 12 underwent attempted surgical drainage and 9 had percutaneous biliary intubation. All 69 patients thought to have resectable disease before surgery underwent exploration: a potentially curative resection was performed in 30, a palliative resection in 3, a drainage procedure in 29, and a biopsy in 7 (see Fig. 1).

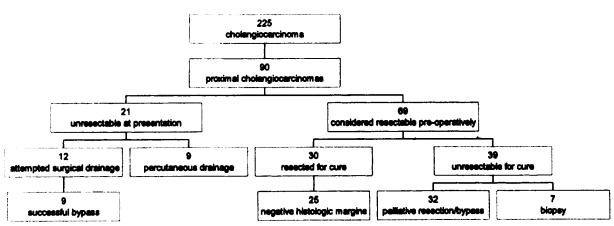

Figure 1. Distribution by treatment of patients with hilar cholangiocarcinoma from March 1, 1991, to April 1, 1997.

Patients With Unresectable Disease

At Presentation

Twenty-three percent (21/90) of the patients were considered to have disease unresectable for cure at presentation, 17 as a result of findings on imaging studies. Reasons for unresectability are summarized in Table 4. In nine patients, local extension precluded a curative resection. Three of the nine had tumor extending to secondary hepatic duct radicles bilaterally, four had portal vein involvement, and two had a combination of the above. Eight patients had metastases seen on either CT scan or ultrasound. Three patients did not undergo resection because of advanced age and coexisting medical conditions. A fourth patient had intractable biliary sepsis and died before complete evaluation.

At Laparotomy

Seventy-seven percent (69/90) of patients were considered to have potentially resectable disease based on presurgical imaging studies. Thirty-nine were found to have unresectable disease at laparotomy (see Table 4). Eight (20%) had locally advanced disease: five had tumor extending to secondary hepatic duct radicles bilaterally, and three who

Table 3. SUMMARY OF CANCER POSITION WITHIN THE BILE DUCT OF 90 PATIENTS WITH PC

Position	n
Left hepatic duct	7
Right hepatic duct	4
Confluence	71
Common hepatic duct	6
Extensive	2
Total	90

PC = percutaneous cholangiography.

Table 4. SUMMARY OF FACTORS PRECLUDING A CURATIVE RESECTION IN PATIENTS AT INITIAL EVALUATION OR AT EXPLORATORY LAPAROTOMY AT MSKCC

Group	n	Local Extension (%)	Nodal Metastases (%)	Distant Metastases (%)	Other* (%)
Unresectable at presentation	21	9	0	8*	4
Unresectable at laparotomy	39	8	14	9	8
Total	60	17 (28)	14 (23)	17 (28)	12 (20)

* Age, comorbidity, sepsis.
† Three additional patients who were unresectable due to local extension on preoperative studies were found to have radiologically occult metastases at laparotomy for palliative bypass.
MSKCC = Memorial Sloan-Kettering Cancer Center.

were thought before surgery to have resectable disease were found to have extensive involvement of the portal vein bifurcation. All five patients with tumor involving secondary hepatic duct radicles had been subjected to biliary intubation before referral.

Fifty-nine percent (23/39) had metastatic disease precluding resection. Fourteen of these 23 patients had gross metastases to either periportal (10/14) or retroperitoneal (4/14) lymph nodes. CT scan indicated lymphadenopathy in four. Nine patients had unsuspected metastatic disease found on exploration: four had omental and/or peritoneal metastases, three had liver metastases, and two had liver and peritoneal metastases.

Five patients, in the judgment of the operating surgeon, were unable to tolerate a curative hepatectomy at the time of exploration: two had cirrhotic livers (unsuspected before surgery), and three had concurrent ischemic heart disease. Three patients who had had surgery elsewhere (one had chemotherapy and radiation before surgery; all three had stents *in situ*) underwent reexploration, but resection could not be performed secondary to inflammation, adhesions, and infection.

Overall

The most common reason for unresectability in all patients was regional lymph node or distant metastatic disease (31/60, 52%). The distribution of distant metastatic spread found by imaging or surgery is summarized in Figure 2. All patients with peritoneal or omental spread had extensive local extension of the primary tumor, and all had liver atrophy with portal vein involvement. Median survival in patients with known M1 disease was 11 ± 3 months. In M0 patients whose disease was unresectable for potential cure, median survival was 11 ± 1.5 months.

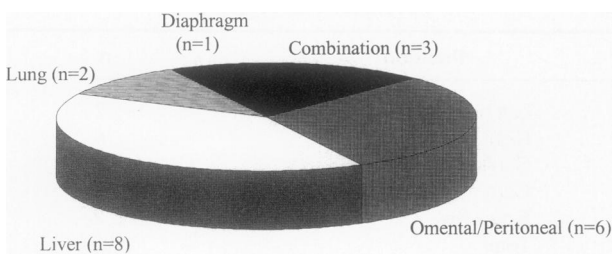

Figure 2. Distribution of distant metastatic spread found on imaging studies or at laparotomy in patients with hilar cholangiocarcinoma.

Resection

Of patients whose disease was considered potentially resectable, 43% (30/69) had resection of all gross tumor in the absence of metastases (R0, R1). Eighty-three percent (25/30) had negative histologic margins at final pathology (R0). The resectability rate of the entire group was 28% (25/90) for R0 resections and 33% (30/90) for R1 resections. Resectability ratios are summarized in Table 5.

Of the 30 patients who underwent a potentially curative resection, 15 had involvement of secondary biliary radicles unilaterally, 11 had unilateral lobar liver atrophy, and 8 had encasement or occlusion of a major portal vein branch (right or left). Twenty-two patients (73%) required partial hepatectomy in addition to bile duct resection to clear gross disease or obtain negative margins on frozen section (Table 6). Nine patients had hepatectomy with partial or total

Table 5. DIFFERENT RESECTABILITY FIGURES FOR PRESENT SERIES

Resection Types	n	%
PCR*/all patients	30/90	33
Resected†/all patients	33/90	37
PCR*/resectable preoperative	30/69	43
Resected†/resectable preoperative	33/69	48
R0‡/all patients	25/90	28
R0/resectable preoperative	25/69	36
R0/PCR	25/30	83

* PCR = potentialy curative resection (R0 and R1).
† includes PCR and palliative resections.
‡ negative histologic margins (R0).

Table 6. SUMMARY OF PROCEDURES PERFORMED IN PATIENTS WITH HILAR CHOLANGIOCARCINOMA UNDERGOING POTENTIALLY CURATIVE RESECTION

Resection Type*	n
Right lobectomy	10
Right hepatectomy, partial caudate resection	2
Right lobectomy with segmental portal vein resection	1
Left hepatectomy, caudate resection	6
Left hepatectomy	2
Left hepatectomy, caudate resection and segmental portal vein resection	1
Bile duct exploration with resection of papillary tumor	1
Bile duct resection	7
Total	30

All patients had concomitant excision of the supraduodenal bile duct, cholecystectomy, and subhilar lymphadenectomy of the hepatoduodenal tissues.[2,3]
* The nomenclature of hepatic resection according to Couinaud.[16]

caudate lobe excision, and two required segmental portal vein resection.

Four of 30 (17%) had positive histologic margins; two of these patients had major liver resections (one right lobectomy and one left hepatectomy with caudate resection). One patient who had an excision of a papillary cholangiocarcinoma had no documentation of a margin and was considered positive. The 30-day mortality rate was 7% and overall survival was 40 months, with a median follow-up time of 26 months (Table 7). When patients were stratified by histologic margin, median survival was significantly longer in patients with histologically negative *versus* positive margins ($p \leq 0.01$, Fig. 3). Of the 25 patients with negative margins, 16 were still alive, with 13 disease-free. Five of these 13 underwent surgery more than 3.5 years ago, during which time all those with positive margins have died of disease. Projected survival exceeded 60 months in patients who underwent resection with negative margins. The 5-year survival rate for all patients who underwent resection was 56%. Patients with positive margins had a median survival greater than those who had surgical bypass (22 months *vs.* 11 months), but this did not reach statistical significance ($p = 0.08$).

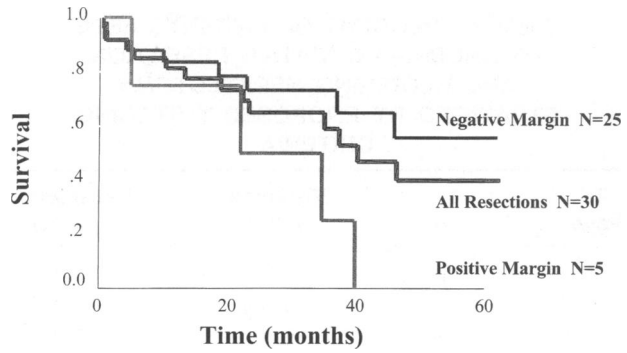

Figure 3. Survival in patients with hilar cholangiocarcinoma who underwent resection of all gross tumor, stratified by histologic margins. Median survival overall (potentially curative resection of all gross disease) was 40 months. The difference in median survival between patients who underwent resection with positive and negative histologic margins was significant ($p \leq 0.01$).

Proposed T-Staging System

In the proposed staging system, resectability was highest in the T1 group (48%) and decreased progressively to 0% in the T4 group (disease was unresectable because of the extent of local disease). There was a significant difference in resectability of disease between patients with T1 disease *versus* those with T3 or T4 disease ($p = 0.05$ and $p = 0.02$, respectively). Fifty-eight percent of patients with T1 disease and 100% of patients with T2 and T3 disease required hepatectomy for removal of gross tumor (Table 8).

On multivariate analysis, portal vein involvement was the only independent predictor of resectability ($p = 0.008$). Hepatic lobar atrophy was closely associated with portal vein involvement and therefore did not emerge as an independent predictor. On the other hand, portal vein involvement, hepatic lobar atrophy, and hepatic ductal extension of tumor (Bismuth–Corlette classification) were independent predictors of the need for partial hepatectomy ($p = 0.001$).

The proposed staging system considers only the extent of the primary tumor and does not take into account the presence of nodal or distant metastases. Nevertheless, the incidence of these findings on presurgical imaging and at laparotomy increased with increasing T stage (Table 9). Thirty percent of patients with T1 disease had metastatic disease

Table 7. SUMMARY OF OPERATIVE MORTALITY AND POST OPERATIVE SURVIVAL IN PATIENTS RESECTED FOR CURE STRATIFIED BY HISTOLOGIC MARGIN

Resection	n	Hepatic Resection (%)	Negative Margin (%)	30-day Mortality (%)	Median Survival	5-yr Survival (%)
PCR	30	22 (73)	25 (83)	2 (6)	40 ± 10	45
Negative margins	25	20 (80)	25	2 (6)	Not reached	56
Positive margins	5	2 (40)	5	0 (0)	22 ± 10*	0

PCR = Potential curative resection.
* $p \leq 0.01$
Median follow-up of 26 months.

Table 8. PERCENT OF PATIENTS ABLE TO UNDERGO CURATIVE RESECTION AND REQUIRING HEPATECTOMY STRATIFIED BY PROPOSED T STAGING CRITERIA

T Stage	n	Resected n (%)	Hepatectomy n (%)
1	40	19 (48)	11 (58)
2	7	3 (43)	3 (100)
3	32	8 (25)	8 (100)
4	8	0	0
Total	87	30 (35)	22 (73)

Table 9. PERCENT OF PATIENTS WITH DISTANT OR NODAL METASTASES FOUND ON PREOPERATIVE SCAN OR AT OPERATION AND SURVIVAL STRATIFIED BY PROPOSED T STAGE

T Stage	n	Metastases n (%)	Median Survival (Months)	5-year Survival (%)
1	40	12 (30)	21 ± 3	20
2	7	1 (14)	35 ± 21	29
3	32	17 (52)	10 ± 2	16
4	8	1 (13)	14 ± 12	0
Total	87			

versus 53% of those with T3 disease (p = 0.05). The proposed staging system also correlated with survival. Median survival in the T1 group was 21 ± 3 months, significantly longer than that in the T3 group (p = 0.05). There was no difference between the T3 and T4 groups. No 5-year survivors were observed in the T4 group (see Table 9).

DISCUSSION

The percentage of patients with hilar cholangiocarcinoma who can undergo a curative resection is difficult to ascertain from the literature. There are two main reasons for this: there is disagreement over what constitutes a curative resection, and most reports lack an absolute denominator consisting of all patients with hilar cholangiocarcinoma at a particular institution.

All agree that complete resection of all gross disease in the absence of metastatic disease is necessary to call a resection potentially curative. The controversy revolves around the significance of histologic margins. Historically, achieving negative histologic margins has been considered nonessential by some because resection of all gross disease stretched the limits of surgical expertise. However, improvements in surgical techniques and presurgical imaging have been accompanied by better results. Table 10 summarizes some of the more recent studies where the percentage of resections achieving negative margins parallels the percentage of patients undergoing partial hepatectomy.

More than 80% of patients in this study who underwent resection of all gross disease had negative histologic margins (R0). Their survival was significantly better than those with positive margins (R1). Other recent series support our results (Table 11). Further, in a recent analysis of prognosis, only histologic margins and nodal disease correlated with survival.[17] There can no longer be any doubt that a negative margin (R0) is necessary to call a resection potentially curative.

At MSKCC, all patients with hilar cholangiocarcinomas are evaluated by a multidisciplinary team; thus, a denominator including patients in all stages of disease is possible. This series indicates that about 25% of all patients with hilar cholangiocarcinoma have inoperable disease at presentation based on radiologic findings. Of the 75% who undergo surgery for a potential resection, less than half can expect to have resection of all gross disease. Approximately one third of all patients in this study were candidates for potentially curative resection (R0), as defined above.

Current radiologic techniques provide adequate imaging of the tumor and its relation to hilar vascular structures[2,13–15] and can be used to predict unresectability secondary to local extent of disease (see Table 1). This observation is substantiated by the results in this study: only 10%

Table 10. HEPATIC RESECTION *VERSUS* HISTOLOGIC MARGINS IN PATIENTS WITH HILAR CHOLANGIOCARCINOMA WHO UNDERWENT RESECTION OF ALL GROSS DISEASE: SUMMATION OF RECENT STUDIES

Author	Year	Period of Study (Years)	PCR* n	Hepatectomy (%)	Negative Margins (%)
Cameron[8]	1990	15	39	20	15
Hadjis[4]	1990	8	27	60	56
Klempnauer[17]	1997	24	147	79	79
Present series	1997	6	30	73	83

* Number of patients undergoing a potentially curative resection (R0, R1).

Table 11. SUMMARY OF STUDIES EVALUATING THE EFFECT OF HISTOLOGIC MARGINS ON SURVIVAL

Author	Year	#PCR* R0	#PCR* R1	R0-Median Survival (mos)	R1-Median Survival (mos)	ps
Present	1997	25	5	Not reached	22	0.01
Pichlmayr[9]	1996	91	27	26	13	0.01
Hadjis[4]	1990	12	15	43	25	0.04

* Number of patients undergoing a potentially curative resection (R0, R1).

of patients were found to have unresectable disease at laparotomy secondary to local spread of disease. Unilateral duct extension, ipsilateral lobar liver atrophy, or involvement of the portal vein bifurcation on presurgical studies did not indicate unresectability; indeed, 50% of patients who underwent resection in this study had one or all of these factors. However, it is more likely that these patients will have unsuspected intraabdominal metastatic spread, as our data indicate.

Hilar cholangiocarcinoma has traditionally been considered a slow-growing, locally invasive tumor. Surprisingly, one third of the patients in this study had metastatic disease precluding curative resection, and 20% had involvement of distant sites. Approximately 10% of distant metastases were diagnosed before surgery, another 10% during surgery. Our surgical findings are supported by the reports by Lai et al.[6] and Cameron et al.,[8] who reported disseminated disease in 11% (10/89) and 15% (14/96) of patients who underwent exploration. Other studies have reported that lymph nodes may be involved in up to one third of patients on exploration.[18–20] This is the first study to document the overall prevalence of metastatic disease precluding curative resection in this population.

Presurgical imaging studies are not accurate in predicting lymph node metastases. Unlike many other cancers, infection (subclinical or clinical cholangitis) is often present in patients with hilar cholangiocarcinoma, leading to adenopathy. This can be misinterpreted as being the result of metastatic spread. On the other hand, less than half the patients with nodal metastases precluding resection had evidence of adenopathy on CT scan.

Two thirds of the distant metastases (lung, liver, omental/peritoneal) were radiologically occult. Small metastatic deposits on the peritoneum or omentum are difficult to appreciate by any imaging technique. As expected, the more substantial discontiguous liver metastases were identified on CT scan, but the scattered smaller ones were missed. Patients with M0 disease who proved to have unresectable disease had a similar survival to those with M1 disease, and only complete resection translated into a survival advantage.

Clearly, better presurgical assessment is necessary. We have previously suggested that any new presurgical staging system should take into account not only the extent of biliary ductal involvement but also the presence and relative laterality of hepatic lobar atrophy and portal venous involvement.[21] The importance of portal vein involvement and liver atrophy in relation to the extent of ductal spread is evident. Thus, ipsilateral involvement of vessels and the bile duct is usually amenable to resection, whereas contralateral involvement is not. The T-staging system herein reported predicts unresectability and allows the staging of resectable lesions with a reasonable indication of the need for partial hepatectomy. Median survival was related to T stage; as T stage increased, so did the incidence of metastases that precluded resection.

The place of laparoscopic assessment in this disease has not been explored, although there is potential for improvement in N and M staging. A recent study that examined the role of laparoscopy in a mixture of hepatobiliary and pancreatic malignancies detected radiologically occult metastases in 30% of patients.[21] The number of these patients who had hilar cholangiocarcinoma was not mentioned. Whether laparoscopy should be performed depends on the philosophy and experience of the surgeon. Almost 90% of patients who had laparotomy in this series underwent a curative resection or palliative bypass procedure. With a median survival of about a year in those who had surgical bypass and 2 years in those who had palliative resections (positive margins), it seems that reliable drainage is necessary to minimize hospital admissions and maximize quality of life.

CONCLUSIONS

The definition of curative or potentially curative resection in hilar cholangiocarcinoma must include negative histologic margins, and hepatectomy is necessary in most cases to achieve this. Unresectability as a result of local factors can be determined before surgery in most patients. Unsuspected metastases account for unresectability in a surprising majority of patients. The proposed T-staging system allows better presurgical selection for therapy and an index of prognosis.

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Discussion

DR. LESLIE H. BLUMGART (New York, New York): The question of the frequency of peritoneal metastases you raised first. I too was surprised when I saw this. In fact, it is unusual in the literature and was unusual as an observation in my previous work. I think Henry Pitt has noticed a similar change, however. You may well be right that this may relate to preoperative manipulation, particularly percutaneous manipulation, allowing bile leakage into the peritoneal cavity.

Incidentally, we are particularly struck by the adverse effects of preoperative drainage in terms of infection. You may have heard the paper that was presented from Memorial at SSO the other day relating to not only high bile duct cancer but also to distal bile duct cancer concerning the adverse infectious complications of previous intervention, particularly endoscopic intubation.

You asked about adjuvant therapy. Yes, I did suggest that once but in fact have not pursued it. Interestingly, we have an antibody for biliary epithelium available now and are just starting a study. One of the aspects that I am particularly interested in is whether radio-immunotherapy might be valuable in patients with positive margins as an adjunct after resection.

The important question you raise is the matter of histologic clearance. And you also refer to hepatectomy rates. I wonder if I could just show one slide which may answer this very well. I took several recent series and put them on this slide, each point representing different series.

Here you see percentage liver resection plotted against negative margins. The higher the percentage of liver resection, the higher is the rate of negative margins; in series with a low incidence of liver resection there is also a low incidence of negative margins. If you look at five-year survival against negative margins, it is completely clear that the achievement of a negative margin is associated with increased survival.

The message is now absolutely clear: Clearance matters and hepatic resection is very frequently necessary for clearance. That is my main message.

DR. RONALD K. TOMPKINS (Los Angeles, California): Since only nine of your 30 resections included the caudate lobe, is it your view that caudate lobe resection is not necessary to treat this disease, as our Japanese colleagues have suggested?

Secondly, there is a problem totally accepting your new classification system as a predictor of resectability, since at the best status in your T system only 48% of the patients were found to be resectable, sort of like flipping a coin.

We do need a staging system. But we need some better predictor of resectability for cure. Your finding that patients who were resected with positive margins did not fare any better than patients who were bypassed is consistent with our findings and those reported by other groups. If we had a better way of predicting who is going to have positive margins before we did a palliative resection, we could put the palliative resection to rest, because it does increase the patients' morbidity and mortality.

Do you use any chemotherapy protocols postoperatively? We have found that this does prolong the survival of our patients who are unresectable, and that is about 70% to 75% of the patients that we treat.

DR. LESLIE H. BLUMGART (New York, New York): Dr. Tompkins, may I take your last question first? No, we haven't been using postoperative chemotherapy.

The question of caudate lobe resection is an interesting one. The Japanese have suggested that this should be routine and is important. I remain to be convinced about the need for routine caudate